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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/688,786	10/17/2003	Henry R. Costantino	1733.2025-003	9558

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EXAMINER

DESAI, ANAND U

ART UNIT	PAPER NUMBER
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1653

DATE MAILED: 01/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No. 10/688,786	Applicant(s) COSTANTINO ET AL.	
	Examiner Anand U. Desai, Ph.D.	Art Unit 1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 19 December 2005.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-22, 24, 25 and 31-40 is/are pending in the application.
- 4a) Of the above claim(s) 36-40 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 31-35 is/are allowed.
- 6) ☒ Claim(s) 1, 2, 12-18, 21, 24 and 25 is/are rejected.
- 7) ☒ Claim(s) 3-11, 19, 20 and 22 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

1. This office action is in response to Amendment filed on December 19, 2005. Claims 23, and 26-30 have been cancelled. Claims 36-40 have been previously withdrawn. Claims 1-22, 24, 25, 31-35 are currently pending and are under examination.

#### **Withdrawal of Rejections**

2. The rejection of claims 1, 2, 5-17, and 19-22 under 35 U.S.C. 103(a) as being unpatentable over Bernstein et al. (U.S. Patent 6,749,866 B2) in view of Lee and Timasheff (Journal of Biological Chemistry Vol. 256, No. 14, pp. 7193-7201 (1981)) is withdrawn.

3. The rejection of claims 3, 4, 18, and 31-35 under 35 U.S.C. 103(a) as being unpatentable over Bernstein et al. (U.S. Patent 6,749,866 B2) in view of Lee and Timasheff (Journal of Biological Chemistry Vol. 256, No. 14, pp. 7193-7201 (1981)) as applied to claims 1, 2, 5-17, and 19-22 above, and further in view of Taylor, K. et al. (Diabetes 51 (suppl. 2):85 Jun 2002) is withdrawn.

4. The rejection of claims 24, and 25 under 35 U.S.C. 103(a) as being unpatentable over Bernstein et al. (U.S. Patent 6,749,866 B2) in view of Lee and Timasheff (Journal of Biological Chemistry Vol. 256, No. 14, pp. 7193-7201 (1981)) as applied to claims 1, 2, 5-17, and 19-22 above, and further in view of Silvestri et al. (U.S. Patent 5,126,147) is withdrawn.

5. The rejection of claims 1, 2, 5-17, and 19-22 under 35 U.S.C. 103(a) as being unpatentable over Woiszwilllo et al. (U.S. Patent 5,981,719) in view of Bernstein et al. (U.S. 6,749,866 B2) is withdrawn.

## **New Objections and Rejections**

### ***Claim Objections***

6. Claim 1 is objected to because of the following informality:

7. The letter, "a" is missing before the words "biologically active polypeptide" in the preamble.

8. Claims 3-11, 19, 20, 22 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Appropriate correction is required.

### ***Claim Rejections - 35 USC § 103***

9. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

10. Claims 1, 2, 12-18, 21, 24, 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bendele et al. (US 2004/0047863 A1) in view of Bernstein et al. (U.S. Patent 6,749,866 B2; cited previously) and Lee and Timasheff (Journal of Biological Chemistry Vol. 256, No. 14, pp. 7193-7201 (1981); cited previously).

Bendele et al. disclose a composition comprising a tumor necrosis factor binding protein (TNFbp) formulated with a controlled release polymer (e.g. a dextran or hyaluronan) with one or more of a corticosteroid, cyclosporine, FK-506, or an interferon and/or an IL-1 inhibitor also formulated with a controlled release polymer (see paragraph, [0175] and [0191]). Bendele et al. does disclose a pharmaceutical preparation, wherein the TNFbp protein is stabilized using

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sucrose (see paragraph [0137]). Bendele et al. does not explicitly disclose the use of salting-out salt and a sugar to stabilize the protein component of the sustained release composition.

Berstein et al. disclose a composition for the modulated release of a biologically active pharmaceutical agent, comprising a biocompatible and biodegradable polymeric matrix, an effective amount of a biologically active pharmaceutical agent, including proteins, and a metal cation component for modulating the release of the biologically active agent from the polymeric matrix, wherein the metal cation is selected from the group consisting of magnesium hydroxide, magnesium carbonate, calcium carbonate, zinc carbonate, magnesium acetate, zinc acetate, magnesium chloride, zinc chloride, magnesium sulfate, zinc sulfate, magnesium citrate, and zinc citrate (see U.S. Patent '866, claim 1). Bernstein et al. teach the stabilization of a protein pharmaceutical agent during the formation of a controlled release polymer matrix composition due to the presence of a polyion chelating the protein. Bernstein et al. describe the controlled release of human growth hormone over a 60 day time period (see Example XII). The polymer is selected from the group consisting of poly(lactide)s, poly(glycolide)s, poly(lactide-co-glycolide)s, polyanhydrides, polyorthoesters, polyetheresters, polycaprolactone, polyesteramides, blends and copolymers thereof (see U.S. Patent '866, claim 2). The biologically active agent is present from about 0.01% (w/w) to about 50% (w/w) of the composition (see U.S. Patent '866, claim 1). Bernstein et al. does not disclose the composition comprising a sugar.

Lee and Timasheff disclose the stabilization of proteins in the presence of sucrose. Circular dichroism and protein absorbance measurements at different temperatures were performed with varying sucrose concentrations to see the effects of sucrose on protein stabilization. The sucrose is preferentially excluded from the protein domain, thereby increasing

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the apparent activation energy of the unfolding process for the protein and thus stabilizing the protein (see Figure 2, Table 2, and Discussion section).

A person having ordinary skill in the art would have used a salt and a sugar to manufacture a controlled release composition, because the state of the art has shown the stabilization of biologically active polypeptides during the manufacturing of sustained release compositions comprising a biocompatible polymer and a biologically active polypeptide with either a salt (see Bernstein et al.) or a sugar, such as sucrose (see Lee and Timasheff). A person having ordinary skill in the art would have expected to succeed in manufacturing a sustained release composition comprising both a salt and a sugar, since both the salt and the sugar are known to stabilize the protein. Applicant is referred to MPEP 2144.06 "Art Recognized Equivalence for the Same Purpose COMBINING EQUIVALENTS KNOWN FOR THE SAME PURPOSE "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (citations omitted) (Claims to a process of preparing a spray-dried detergent by mixing together two conventional spray-dried detergents were held to be prima facie obvious.)."

### *Conclusion*

11. Claims 1, 2, 12-18, 21, 24, 25 are rejected.
12. Claims 3-11, 19, 20, and 22 are objected.
13. Claims 31-35 are allowable.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anand U. Desai, Ph.D. whose telephone number is (571) 272-0947. The examiner can normally be reached on Monday - Friday 7:00 a.m. - 3:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on (517) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

January 23, 2006



**JON WEBER**  
**SUPERVISORY PATENT EXAMINER**